

Thomas Krahn et al.  
Application No. 09/966,522  
Amendment Under 37 CFR § 1.111  
Reply to Office Action of October 1, 2004

**CONDITIONAL PETITION FOR EXTENSION OF TIME**

If entry and consideration of the amendments above requires an extension of time, Applicants respectfully request that this be considered a petition therefor. The Commissioner is authorized to charge any fee(s) due in this connection to Deposit Account No. 14-1263.

**ADDITIONAL FEE**

Please charge any insufficiency of fees, or credit any excess, to Deposit Account No. 14-1263.

**REMARKS/ARGUMENTS**

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

At the outset, Applicants point out that they will file on the next business day an information disclosure statement citing one new reference which may be of relevance to the instant application. In case the information disclosure statement has not been matched with the file at the time that the Examiner picks up the file for action, Applicants respectfully request that the Examiner try to locate the information disclosure statement, and, if it cannot be located, that the Examiner contact the undersigned at telephone number 212-808-0700 so that a duplicate

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copy of the information disclosure statement can be provided.

Turning to the open Office Action, Applicants acknowledge with appreciation the Examiner's indication that Applicants' arguments in traversal of the restriction requirement were persuasive. Applicants are a bit confused, however, in that claims 6-16 and 24-42 remain withdrawn from consideration. Applicants believe that if Applicants' arguments were persuasive, claims 6-16 and 24-42 should have been rejoined and examined on the merits. Applicants respectfully request that the Examiner clarify the status of claims 6-16 and 24-42 in the next Office Action. Applicants also point out that claims 1-5 have been canceled.

Claim 22 was rejected under 35 USC § 112, first paragraph, as claiming new matter. In response, Applicants have amended claim 22 to recite that Brilliant Black is the *masking* dye.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has been reconsidered and withdrawn is, therefore, earnestly solicited.

Claim 22 was rejected under 35 USC § 103(a) as being obvious over Cubbage et al. ("Cubbage"), U.S. Patent No. 5,582,982. In response, Applicants believe the amendment to claim 22 to recite Brilliant Black is the masking dye moots this rejection.

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In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has been reconsidered and withdrawn is, therefore, earnestly solicited.

Claims 17-21 and 23 were rejected under 35 USC § 102(e) as being anticipated by Cubbage. In response, Applicants would remind the Examiner that anticipation requires that each and every element as set forth in the claim must be found, either expressly or inherently described, in a single prior art reference, and, further, if the Examiner relies on a theory of inherency as to any particular element, then the extrinsic evidence must make clear that such element is *necessarily* present in the thing described in the reference, and the presence of such element therein would be so recognized by persons skilled in the art. *In re Robertson*, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Further, inherency is not established by probabilities or possibilities, and the mere fact that a property may result from a given circumstances is not sufficient; instead it must be shown that such property *necessarily* inheres in the thing described in the reference. *Id.* In response, Applicants submit that Cubbage does not teach each and every limitation of the rejected claims, and, therefore, also that Cubbage does not anticipate the present claims.

Instant claim 17 requires that (1) the "masking dye is substantially impermeant to the

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membrane of a biological cell” and (2) the “masking dye does not specifically bind to [a] membrane of [a] biological cell.” The other rejected claims incorporate these same requirements by their dependence on claim 17.

Cubbage expressly teaches, for example, at column 3, lines 41-43, that “the background-reducing compound will diffuse *onto and into* the biological entity (emphasis added.)” In the case where the biological entity is, for example, a cell, this means that the background-reducing compound will bind to the target cell and will also substantially penetrate the membrane of the target cell to be incorporated inside said target cell.

These actions are not permitted according to instant claim 17 and the rejected claims dependent thereon. Consequently, Cubbage cannot possibly anticipate any of the rejected claims.

In the third paragraph on page 6 of the Office Action, the Examiner writes:

“First, the limitation of ‘the masking dye (sic) is substantially impermeant to the membrane of the biological cell’ is a functional limitation of the composition being claimed.”

This is true to an extent. The rejected claims are not drawn to a composition, but, rather, to a kit for performing a biomedical assay. However, Applicants agree that the limitation “the

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masking dye is substantially impermeant to the membrane of the biological cell” is a functional limitation. Nevertheless, Applicants point out that it is improper for the Examiner to ignore any limitation, including functional limitations. As set forth in MPEP § 2173.05(g):

“A functional limitation *must* be evaluated and considered, *just like any other limitation of the claim*, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used.”

[Emphasis added.]

However, the Examiner next states:

“Since Applicants fail to define specific masking dye, any masking dye in the reference would satisfy the requirement of a masking dye.”

This is true only if *every* masking dye in the reference is also substantially impermeant to the membrane of the biological cell. If every masking dye in the reference is *not* substantially impermeant to the membrane of the biological cell, then the reference cannot anticipate the instant claims, which require such substantial impermeance. To the extent that the Examiner is saying that because Applicants did not recite a specific masking dye, the Examiner may ignore the functional requirement that the masking dye be impermeant to the membrane of the biological cell, this is absolutely false, and contrary to law. As noted above, the functional

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limitation *must* be evaluated and considered for what it conveys to a person of ordinary skill in the art. Such persons would understand that a dye that is intended to be completely permeable, such as Cubbage's dye, does not meet the instantly claimed requirement of being substantially impermeant.

However, the Examiner next states:

"And if such masking dye reduces non-specific background when combined with a fluorescent dye, then it would have other functional limitations such as being impermeant to the biological cell."

This does not follow, and has no support whatsoever on the record. This statement totally ignores the fact that Cubbage's invention and the instant invention operate in fundamentally different manners. In Cubbage's invention, the background-reducing compound absorbs light from nonspecifically bound probe or autofluorescing molecules better than the background-reducing compound absorbs light from specifically bound probe. See, column 4, lines 4-8. Thus, Cubbage desires that the background-reducing compound *penetrate* the cell membrane to reduce any nonspecifically bound probe *inside the cell*. In this regard, Cubbage teaches at column 3, lines 60-65, that the background-reducing compound and the nonspecifically bound probe should be in close proximity for background reduction.

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In contrast, according to the teachings of the present invention, the masking dye is substantially impermeant and does not specifically bind to the cell membrane, and, therefore, the masking dye masks nonspecific fluorescence *from outside the cell*, i.e., from the solution or the container. It does not mask nonspecific fluorescence from inside the cell.

Respectfully, the Examiner's position on this point is untenable. While the use of the functional language "substantially impermeant" affords Applicants' some leeway, no reasonable construction of "substantially impermeant" covers a completely "permeant" dye of the type contemplated by Cubbage. No person having ordinary skill in the art would read Cubbage as contemplating substantially impermeant masking dyes. As indicated above, Cubbage clearly contemplates a completely permeant dye, which gets inside the cell, and masks from the inside. Consequently, a person having ordinary skill in the art would understand that Cubbage's invention is not embraced by the instant claims. Respectfully, the Examiner is constrained to follow the understanding of persons skilled in the art.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection also. An early notice that this rejection has been reconsidered and withdrawn is, therefore, earnestly solicited.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding

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objections and rejections.

Applicants further believe that this application is in condition for immediate allowance. However, should the Examiner determine that any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,  
NORRIS MCLAUGHLIN & MARCUS, P.A.

By

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that the foregoing Amendment under 37 CFR § 1.111 and the accompanying Petition for Extension of Time (21 pages total) are being facsimile transmitted to the United States Patent and Trademark Office on the date indicated below:

Date: April 1, 2005

By:

Kurt G. Briscoe

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